UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,555	01/09/2001	Levon Michael Khachigian	273402002020	9700

25226 7590 08/24/2005

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,555	KHACHIGIAN, LEVON MICHAEL	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

2. The rejection of claims 1-2 and 4-9 is withdrawn in response to Applicant's amendment canceling claims 8-9, and in response to Applicant's arguments submitted 6-01-05. However, a new grounds of rejection is set forth below.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2 and 4-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendelsohn et al. in view of Sells et al.

Mendelsohn et al. provides screening methods that can be used to identify vasoprotective agents, which inhibit vascular smooth muscle cell activation and/or proliferation or enhance vascular endothelial cell activation and/or proliferation or activate estrogen responsive genes in vascular cells. One type of screening assay described in this reference involves examining the effect of a candidate vasoproctective agent on reporter constructs to indirectly monitor the effect of the agent on the proliferation and/or activation of vascular cells and to monitor the effect of an agent on the expression of an estrogen responsive gene. In one specific embodiment of this invention, Mendelsohnn et al. describe the use of a reporter construct comprising an estrogen

receptor responsive gene, wherein preferred vasoprotective agents are identified by their ability to influence the expression of an estrogen responsive gene. For example, in each of the following cases the format ("+" or "-") describes the preferred response in vascular endothelial cells / preferred response in vascular smooth muscle cells: prostaglandin cyclooxygenase (+/+), prostaglandin synthase (+/+), nitric oxide synthase (constitutive or calcium-dependent) (+/+), collagen (-/-), elastin (-/-), c-fos (+/-), progesterone receptor (+/+), vascular endothelial growth factor (+/+), epidermal growth factor receptor (-/-), interleukin-6 (+/+), neu (-/-), egr-1 (-/-), estrogen receptor (+/+), heat shock protein 27 (+/-), vascular adhesion molecules (-/-), vascular smooth muscle cell calcium channels (-/-), ryanodine receptor (-/-), FLT4 receptor tyrosine kinase (+/-), fibroblast growth factor receptor (-/-), and inducible nitric oxide synthase (+/+). Therefore, (+/+) refers to wherein indicates that the preferred agents increase expression of that gene (or a reporter operably linked to the upstream control region of that gene in the indicated cell type), and (-/-) refers to the ability of the preferred agent to inhibit or decrease expression of said gene or reporter gene (col. 11, lines 37-54).

Mendelsohnn et al. does not explicitly describe a method of screening for compounds that inhibit proliferation of cells selected from vascular smooth muscle cells or endothelial cells, wherein the method specifically comprises determining the ability of a putative compound to inhibit induction of egr-1.

Absent evidence to the contrary, one of ordinary skill in the art at the time of filing of the instant application seeking alternative means for identifying potential vasoprotective agents, and in view of the teachings of Mendelsohnn et al., would have been motivated to design a reporter construct comprising either the egr-1 gene as a reporter gene or comprising the upstream

regulatory sequence of egr-1 in combination with another reporter gene, to be used in a method for identifying compounds that inhibit proliferation of cells by determining the ability of said compound to inhibit or decrease the expression of the egr-1 reporter construct. It would have been obvious to one of ordinary skill in the art to modify the teachings of Mendelsohnn et al. to design the methods of the claimed invention since Mendelsohnn et al. clearly teach that "any gene which is responsive to an estrogen receptor can serve as the basis for a reporter construct (col. 11, lines 22-23)," wherein said reporter constructs are "used to indirectly monitor the effect of an agent on the proliferation and/or activation of vascular cells and to monitor the effect of an agent on the expression of an estrogen responsive gene (col. 11, lines 12-15)." Mendelsohnn et al. goes on to describe vascular genes of interest to be used in said reporter constructs, wherein the list of vascular genes comprises the "egr-1" gene (col. 11, lines 29). Additionally, Mendelsohnn et al. specifically teaches that the expected effect of the potential vasoproctective agent on the expression of egr-1 is a decrease (-/-) in expression of egr-l in both vascular smooth muscle cells and vascular endothelial cells (col. 11, lines 46-54).

5. The invention of Mendelsohnn encompasses other alternative embodiments of vasoprotective agents, for example, at col. 1, lines 43-63, it states that the present invention relates to a screening method that can be used to identify agents which inhibit vascular smooth muscle cell activation and/or proliferation or enhance vascular endothelial cell activation and/or proliferation or activate estrogen responsive genes in vascular cells. Therefore, there are several classes of vasoprotective agents described by this reference. Moreover, at col. 11, lines 37-59, it states that preferred vasoprotective agents decrease the expression of egr-l, as indicated by egr-l

(-/-) (see col. 11, line 54). In this case the term "(-/-)" is defined as "(preferred response in vascular endothelial cells/preferred response in vascular smooth muscle cells)."

6. It is not specifically indicated in this passage that the overall effect of decreasing egr-1 expression in these cells is inhibition of vascular endothelial and vascular smooth muscle cell proliferation.

7. Sells et al. teach the use of an antisense oligonucleotide targeting EGR-1 mRNA to reduce the expression of EGR-1 in melanoma cells. It was concluded that inhibition of EGR-1 in melanoma cells by antisense or dominant negative mutants of EGR-1 block the effects of EGR-1 on IL-1 activity, and leads to IL-1 induced tumor growth arrest. Therefore, Sells et al. teach that inhibitors of EGR-1 function to inhibit the proliferation of tumor cells.

It would have been obvious to one of ordinary skill in the art to test the ability of the candidate vasoprotective agent for its ability to function as a vasoprotective agent in vascular endothelial cells and smooth muscle cells by utilizing the assay described in Mendelsohnn et al. (see col. 12-13). Moreover, it would have been obvious to one or ordinary skill in the art at the time of the instant invention to combine the teachings of Mendelsohn et al. with the teachings of Sells et al. in the design of the instant invention which comprises an additional step of testing the ability of the putative Egr-1 inhibitor to inhibit the proliferation of cells. One of ordinary skill in the art would have been motivated to make this modification since it is clear that the prior art teaches the function of Egr-1 in the regulation of cell proliferation as per the teaching of Sells et al., and further teaches that inhibitors of Egr-1 function to inhibit the proliferation of tumor cells.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571)272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1633

JLE